Access DB# 89911

SEARCH REQUEST FORM

RECEIVED

MAR 25 2003

Scientific and Technical Information Center

Requester's Full Name: Molly Oeperley Examiner #: 59757 Date: 03/25/03
Art Unit: 1641 Phone Number 30 8-4239 Serial Number: 09/889 713
Mail Box and Bldg/Room Location: 8D15 Results Format Preferred (circle): PAPER DISK E-MAIL
↳ 7E12

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Selective labeling + isolation of phosphopeptides and applications to proteome analysis

Inventors (please provide full names): Ruedi Aebersold, Huilin Zhou

Point of Contact
Susan Hanley
Technical Info. Specialist
CM1 6B05 Tel: 305-4053

Earliest Priority Filing Date: 06/12/00

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

① Please search for the labeling of phosphate groups in a phosphoprotein or phosphopeptide as described in claim 1.

Involves formation of phosphoramide bond (to protect phosphate group), protection of carboxylic acid group by formation of amide bond (specifically carboxyamidate bond). Uses ethanolamine for this step (claim 7).

Involves cleavage of phosphoramide bond to regenerate free phosphate groups. Uses trifluoroacetic acid for this step (claim 8).

Optionally further involves reacting the free phosphate group with cystamine (see claim 10).

Optionally involves a solid support. Sea glass beads with iodoacetyl groups of claim 13.
↳ controlled pore glass (CPG)

Terms: proteome, protein analysis, label?, tag?, mass spectrometry (claim 34), isotope proteomics
↳ fluoresc?, radio?, colorimetric, affinity (claim 15)

L1

STAFF USE ONLY		Type of Search		Vendors and cost where applicable	
Searcher:	Hanley	NA Sequence (#)		STN	
Searcher Phone #:		AA Sequence (#)		Dialog	
Searcher Location:		Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	3/27	Bibliographic	X	Dr.Link	
Date Completed:	4/2	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:		Fulltext		Sequence Systems	
Clerical Prep Time:		Patent Family		WWW/Internet	
Online Time:		Other		Other (specify)	

PTO-1590 (8-01)

Inventor Search


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=> d his

     (FILE 'HOME' ENTERED AT 10:27:26 ON 02 APR 2003)

     FILE 'HCAPLUS' ENTERED AT 10:27:37 ON 02 APR 2003
L1           291 S AEBERSOLD R?/AU
L2          4434 S ZHOU H?/AU
L3             8 S L1 AND L2
L4             6 S L3 AND LABEL?
L5          4717 S L1-2
L6           410 S L5 AND PHOSPH?
L7            26 S L6 AND (LABEL? OR TAG OR TAGGING OR TAGGED)
L8            24 S L7 AND PROT?
L9             2 S L3 AND L8
L10            6 S L3 NOT L9
                 SELECT RN L9 1-2

     FILE 'REGISTRY' ENTERED AT 10:31:27 ON 02 APR 2003
L11           28 S E1-28

     FILE 'HCAPLUS' ENTERED AT 10:31:32 ON 02 APR 2003
L12            2 S L9 AND L11   2 cites w/ 28 cpds displayed
                 SELECT RN L10 1-6

     FILE 'REGISTRY' ENTERED AT 10:33:48 ON 02 APR 2003
L13           12 S E29-40

     FILE 'HCAPLUS' ENTERED AT 10:33:58 ON 02 APR 2003
L14            4 S L13 AND L10
L15            6 S L10 OR L14   6 cites w/ 12 cpds displayed
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Considered 05/01/03

=> d ibib abs hitstr ind 1

L12 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:869473 HCAPLUS
DOCUMENT NUMBER: 137:365991
TITLE: Methods for isolation and **labeling** of sample molecules using solid supports coupled to reactive, cleavable, and **tagging** functional groups
INVENTOR(S): **Aebersold, Rudolf H.; Zhou, Huilin**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002168644	A1	20021114	US 2001-858198	20010514
WO 2002093131	A2	20021121	WO 2002-US15500	20020514

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

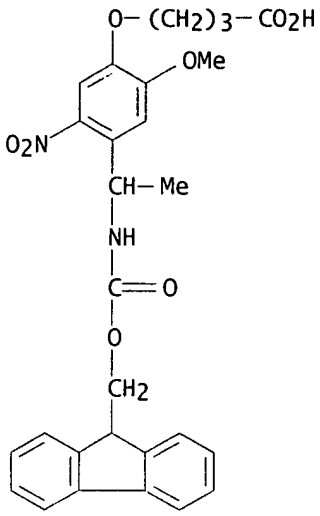
PRIORITY APPLN. INFO.: US 2001-858198 A1 20010514

AB The invention provides methods for **labeling** a mol. by contacting a sample mol. with a solid support coupled to a chem. group comprising a cleavable functional group, one or more functional groups, and a reactive group for the sample mol., under conditions allowing the sample mol. to covalently bind to the reactive group; and cleaving the cleavable functional group, thereby releasing the sample mol. comprising the one or more functional groups, which can be a **tag**. The invention also provides a solid support covalently coupled to a chem. group comprising a cleavable functional group, a mass spectrometry **tag** and a reactive group for covalently attaching a sample mol., wherein the cleavable functional group, the **tag** and the reactive group are positioned relative to each other to allow transfer of the **tag** to the sample mol. upon cleavage of the cleavable functional group. Glass beads were functionalized with amino groups, reacted with Fmoc **protected** photolinker [4-[4-[1-(Fmocamino)ethyl]-2-methoxy]-5-nitrophenoxy]butanoic acid, deprotected and reacted with iodoacetic anhydride. Cysteine-contg. laminin B peptide was reduced by tris(2-carboxyethyl)**phosphine** and reacted with the reactive glass beads. The beads were washed and exposed to UV light for photocleavage. The leucine-**labeled** peptide was detected by mass spectrometry.

IT **162827-98-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Fmoc-**protected** photolinker, in prepn. of reactive support beads; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

RN 162827-98-7 HCAPLUS

CN Butanoic acid, 4-[4-[1-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]ethyl]-2-methoxy-5-nitrophenoxy]- (9CI) (CA INDEX NAME)



IT **7782-39-0**, Deuterium, analysis
RL: ARU (Analytical role, unclassified); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(amino acid **tag** contg.; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
RN 7782-39-0 HCAPLUS
CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D—D

IT **7726-95-6**, Bromine, analysis **7782-50-5**, Chlorine, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(functional group contg.; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
RN 7726-95-6 HCAPLUS
CN Bromine (8CI, 9CI) (CA INDEX NAME)

Br—Br

RN 7782-50-5 HCAPLUS
CN Chlorine (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Cl—Cl

IT **474759-87-0P**
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

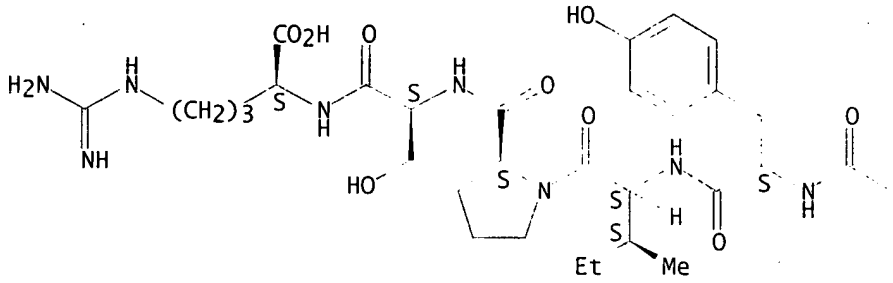
(isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

RN 474759-87-0 HCAPLUS

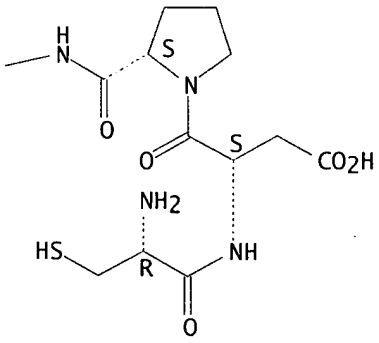
CN L-Arginine, L-cysteinyl-L-.alpha.-aspartyl-L-prolylglycyl-L-tyrosyl-L-isoleucyl-L-prolyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



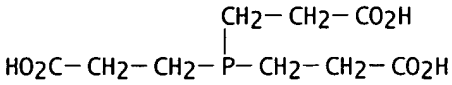
PAGE 1-B



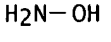
IT **5961-85-3DP**, Tris(2-carboxyethyl)**phosphine**, reaction products with polypeptide **7803-49-8DP**, Hydroxylamine, reaction products with polypeptide **76931-93-6DP**, N-Succinimidyl S-acetylthioacetate, reaction products with polypeptide
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

RN 5961-85-3 HCAPLUS

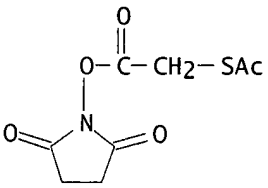
CN Propanoic acid, 3,3',3''-phosphinidynetris- (9CI) (CA INDEX NAME)



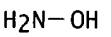
RN 7803-49-8 HCAPLUS
CN Hydroxylamine (8CI, 9CI) (CA INDEX NAME)



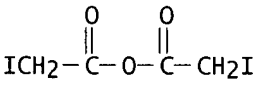
RN 76931-93-6 HCAPLUS
CN Ethanethioic acid, S-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethyl] ester (9CI) (CA INDEX NAME)



IT **7803-49-8**, Hydroxylamine, reactions **54907-61-8**, Iodoacetic anhydride **129785-85-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
RN 7803-49-8 HCAPLUS
CN Hydroxylamine (8CI, 9CI) (CA INDEX NAME)



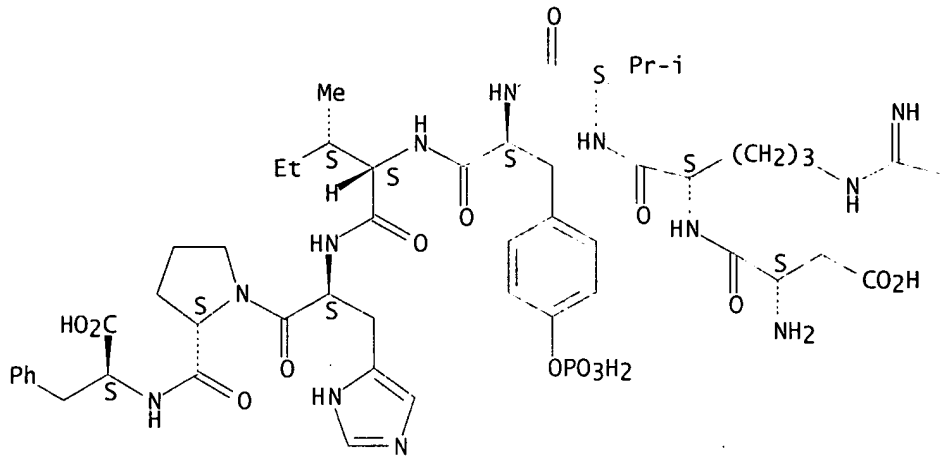
RN 54907-61-8 HCAPLUS
CN Acetic acid, iodo-, anhydride (6CI, 9CI) (CA INDEX NAME)



RN 129785-85-9 HCAPLUS
CN Angiotensin II, 5-L-isoleucine-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

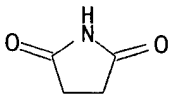
PAGE 1-A



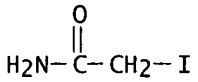
PAGE 1-B

IT **60267-61-0DP**, Ubiquitin, conjugates with polypeptides
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(**labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
RN 60267-61-0 HCAPLUS
CN Ubiquitin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **123-56-8D**, Succinimide, esters **144-48-9**, Iodoacetamide
RL: ARU (Analytical role, unclassified); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(reactive group contg.; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
RN 123-56-8 HCAPLUS
CN 2,5-Pyrrolidinedione (9CI) (CA INDEX NAME)

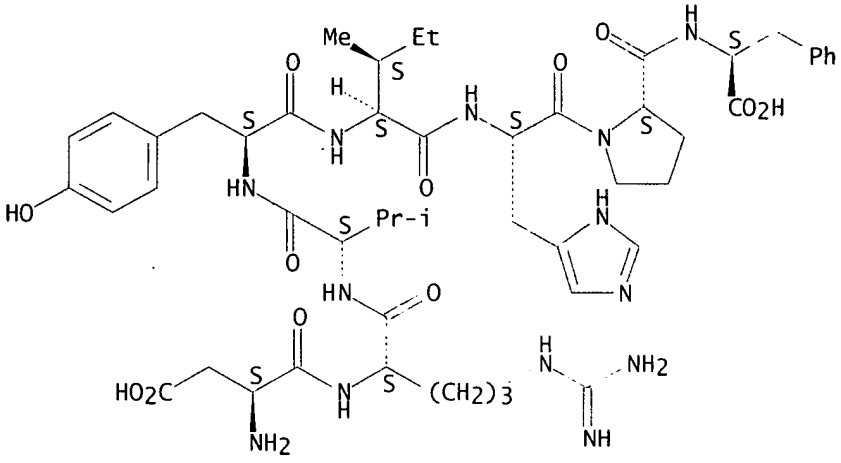


RN 144-48-9 HCAPLUS
CN Acetamide, 2-iodo- (8CI, 9CI) (CA INDEX NAME)



IT **4474-91-3**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(unclaimed sequence; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
RN 4474-91-3 HCAPLUS
CN Angiotensin II, 5-L-isoleucine- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C12Q001-68
ICS G01N033-53; C12P021-06; C12P019-34
NCL 435006000
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 34
ST **labeling** mol reactive cleavable functional group; mass spectrometry **tag labeling** support
IT Laminins
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(B; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
IT **Proteins**
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(acetylated, **labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)
IT Animal tissue
Cell

Plant tissue
(anal. of classes of mols. of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Glass beads
RL: RCT (Reactant); RACT (Reactant or reagent)
(as solid support; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Chromophores
Fluorescent substances
Spin **labels**
(as **tags**; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Isotopes
RL: ARU (Analytical role, unclassified); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(as **tags**; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Amino acids, analysis
RL: ARU (Analytical role, unclassified); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(charged, as **tags**; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Peptides, preparation
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(cysteine-contg.; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **Proteins**
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(hydroxylated, **labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Antibodies
RL: NUU (Other use, unclassified); USES (Uses)
(in polypeptide isolation; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Analysis
Functional groups
Molecules
Process automation
(isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Lipoproteins
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(isoprenoid-contg., **labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Second messenger system
(**labeling** of messenger from; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable,

and **tagging** functional groups)

IT Metabolism
(**labeling** of metabolite from; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Glycopeptides
Glycoproteins
Lipids, analysis
Nucleic acids
Peptides, analysis
Phosphopeptides
Phosphoproteins
Proteins
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(**labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Light
(linker cleavable by; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Enzymes, uses
RL: CAT (Catalyst use); NUU (Other use, unclassified); USES (Uses)
(linker cleavable by; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Acids, uses
Bases, uses
RL: NUU (Other use, unclassified); USES (Uses)
(linker cleavable by; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Mass spectrometry
(liq. chromatog. combined with; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Liquid chromatography
(mass spectrometry combined with; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **Proteins**
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(myristylated, **labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Hydrophobicity
(of **tag**; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **Proteins**
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(palmitylated, **labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Functional groups
(pyridyl, as **tags**; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and

tagging functional groups)

IT **Proteins**
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(sulfoproteins, **labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Solids
(supports; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT Mass spectrometry
(**tags**; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **162827-98-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Fmoc-**protected** photolinker, in prepn. of reactive support beads; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **7782-39-0**, Deuterium, analysis
RL: ARU (Analytical role, unclassified); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(amino acid **tag** contg.; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **7726-95-6**, Bromine, analysis **7782-50-5**, Chlorine, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(functional group contg.; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **474759-87-0P**
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **5961-85-3DP**, Tris(2-carboxyethyl)**phosphine**, reaction products with polypeptide **7803-49-8DP**, Hydroxylamine, reaction products with polypeptide **76931-93-6DP**, N-Succinimidyl S-acetylthioacetate, reaction products with polypeptide
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **7803-49-8**, Hydroxylamine, reactions **54907-61-8**, Iodoacetic anhydride **129785-85-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **60267-61-0DP**, Ubiquitin, conjugates with polypeptides
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(**labeling** of; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **123-56-8D**, Succinimide, esters **144-48-9**, Iodoacetamide
RL: ARU (Analytical role, unclassified); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(reactive group contg.; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

IT **4474-91-3**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(unclaimed sequence; isolation and **labeling** of sample mols. using solid supports coupled to reactive, cleavable, and **tagging** functional groups)

=> d ibib abs hitstr ind 2

L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:924099 HCAPLUS
DOCUMENT NUMBER: 136:50669
TITLE: Selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** analysis
INVENTOR(S): Aebersold, Ruedi; Zhou, Hu[illegible]
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096869	A1	20011220	WO 2001-US18988	20010612
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1295123	A1	20030326	EP 2001-944486	20010612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002049307	A1	20020425	US 2001-880713	20011018
PRIORITY APPLN. INFO.:			US 2000-210972P P	20000612
			WO 2001-US18988 W	20010612

this applicn.

AB A method for selective **labeling** of **phosphate** groups in natural and synthetic oligomers and polymers in the presence of chem. related groups such as carboxylic acid groups. The method is specifically applicable to biol. oligomers and polymers, including **phosphopeptides**, **phosphoproteins** and **phospholipids**. In a specific embodiment, selective **labeling** of **phosphate** groups in **proteins** and peptides, for example, facilitates sepn., isolation and detection of **phosphoproteins** and **phosphopeptides** in complex mixts. of **proteins**. Selective **labeling** can be employed to selectively introduce **phosphate labels** at **phosphate** groups in an oligomer or polymer, e.g., in a peptide or **protein**. Dection of the presence of the **label**, is used to detect the presence of the **phosphate** group in the oligomer or polymer. The method is useful for the detection of **phosphoproteins** or **phosphopeptides**. The **phosphate label** can be a colorimetric **label**, a radiolabel, a fluorescent or **phosphorescent label**, an affinity **label** or a linker group carrying a reactive group (or latent reactive group) that allows selective attachment of the oligomer of polymer (**protein** or peptide) to a **phosphate label**, to an affinity **label** or to a solid support. The method can be combined with well-known methods of mass spectrometry to detect and identify **phosphopeptides** and **phosphoproteins**

IT **9001-04-1**, Pyruvate decarboxylase
RL: ANT (Analyte); ANST (Analytical study)
(isoenzyme 1; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
RN 9001-04-1 HCAPLUS
CN Decarboxylase, pyruvate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9001-41-6**, Glucose 6-**phosphate** isomerase
9001-50-7, Glyceraldehyde 3- **phosphate** dehydrogenase
9001-59-6, Pyruvate kinase **9001-60-9**, L-Lactate dehydrogenase **9001-83-6**, **Phosphoglycerate** kinase
9014-08-8, Enolase **9024-52-6**, Aldolase **9032-62-6**
, **Phosphoglycerate** mutase
RL: ANT (Analyte); ANST (Analytical study)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
RN 9001-41-6 HCAPLUS
CN Isomerase, glucose phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-50-7 HCAPLUS
CN Dehydrogenase, glyceraldehyde phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-59-6 HCAPLUS
CN Kinase (phosphorylating), pyruvate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-60-9 HCAPLUS
CN Dehydrogenase, lactate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-83-6 HCAPLUS
CN Kinase (phosphorylating), phosphoglycerate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9014-08-8 HCAPLUS
CN Hydratase, phosphoenolpyruvate (9CI) (CA INDEX NAME)

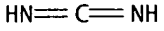
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9024-52-6 HCAPLUS
CN Aldolase, fructose diphosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9032-62-6 HCAPLUS
CN Phosphomutase, glycerate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **7782-39-0**, Deuterium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
RN 7782-39-0 HCAPLUS
CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D-D

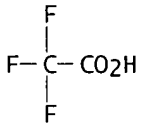
IT **151-51-9**, Carbodiimide **9002-07-7**, Trypsin
RL: CAT (Catalyst use); USES (Uses)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
RN 151-51-9 HCAPLUS
CN Methanediimine (9CI) (CA INDEX NAME)



RN 9002-07-7 HCAPLUS
CN Trypsin (8CI, 9CI) (CA INDEX NAME)

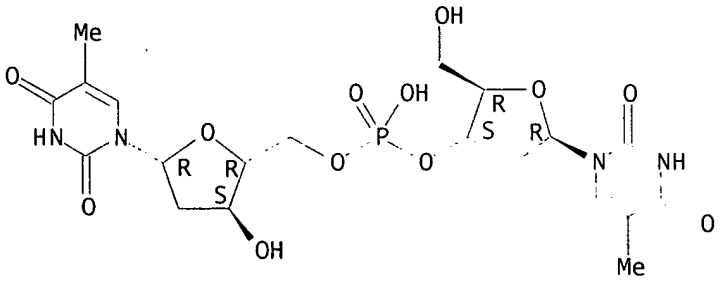
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **51-85-4**, Cystamine **76-05-1**, Trifluoroacetic acid, reactions **1969-54-6 7803-49-8**, Hydroxyamine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
RN 51-85-4 HCAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)

RN 76-05-1 HCAPLUS
CN Acetic acid, trifluoro- (8CI, 9CI) (CA INDEX NAME)



RN 1969-54-6 HCAPLUS
CN Thymidine, thymidylyl-(3'.fwdarw.5')- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 7803-49-8 HCAPLUS
CN Hydroxylamine (8CI, 9CI) (CA INDEX NAME)

H_2N-OH

IC ICM G01N033-53
ICS G01N033-543; G01N031-00; G01N033-00; G01N021-76; G01N021-62; G01N001-00; G01N001-18; G01N033-537; C07K001-00; C12N011-02; C12P021-08; C12Q001-37
CC 9-16 (Biochemical Methods)
ST **labeling** isolation **phosphopeptide proteome** analysis
IT Ribosomal **proteins**
RL: ANT (Analyte); ANST (Analytical study)
(40s; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Ribosomal **proteins**
RL: ANT (Analyte); ANST (Analytical study)
(60s; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Condensation reaction
(Carbodiimide-catalyzed; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Functional groups
(Ethanolamine; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Functional groups
(Hydroxy acid; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Functional groups
(Iodoacetyl; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Liquid chromatography
(Microcapillary; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Bond
(**Phosphoramide**; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Materials
(Solid phase; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Bond
(covalent; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT **Proteins**
RL: ANT (Analyte); ANST (Analytical study)
(human GAP SH3 binding; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Standard substances, analytical
(internal; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Carboxyl group
(ionized; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT **Phosphoproteins**
RL: ANT (Analyte); ANST (Analytical study)
(p19; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT Amino acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(**phosphates**; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Affinity
Amide group
Amino group
Bond cleavage
Chemicals
Colorimetric indicators
Fluorescence
Fluorescent indicators
Functional groups
Immobilization, molecular
Isotope indicators
Labels
Linking agents
Mass spectrometry
Mixtures
Nutrition, animal
Phosphate group
Phosphorescent substances
Protective groups
Protein sequences
Reaction
Reducing agents
Reduction
Samples
Separation
Sulfhydryl group
Tandem mass spectrometry
Test kits
Yeast
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Heat-shock **proteins**
RL: ANT (Analyte); ANST (Analytical study)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT **Proteome**
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT **Phospholipids**, analysis
Phosphopeptides
Phosphoproteins
RL: ANT (Analyte); PUR (Purification or recovery); RCT (Reactant); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Enzymes, uses
RL: CAT (Catalyst use); USES (Uses)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Glass beads
RL: NUU (Other use, unclassified); USES (Uses)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)
IT Acids, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT Biopolymers
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT Oligomers
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT Peptides, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT Polymers, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT **Proteins**
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT mRNA
RL: ANT (Analyte); ANST (Analytical study)
(thyroid hormone receptor-assocd. **protein** complex component TRAP150; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT **Proteins**
RL: ANT (Analyte); ANST (Analytical study)
(tumor necrosis factor type 1 receptor assocd.; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT Caseins, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.-; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT **9001-04-1**, Pyruvate decarboxylase
RL: ANT (Analyte); ANST (Analytical study)
(isoenzyme 1; selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT **9001-41-6**, Glucose 6-**phosphate** isomerase **9001-50-7**, Glyceraldehyde 3- **phosphate** dehydrogenase **9001-59-6**, Pyruvate kinase **9001-60-9**, L-Lactate dehydrogenase **9001-83-6**, **Phosphoglycerate** kinase **9014-08-8**, Enolase **9024-52-6**, Aldolase **9032-62-6**, **Phosphoglycerate** mutase
RL: ANT (Analyte); ANST (Analytical study)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT **7782-39-0**, Deuterium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective **labeling** and isolation of **phosphopeptides** and applications to **proteome** anal.)

IT **151-51-9**, Carbodiimide **9002-07-7**, Trypsin
RL: CAT (Catalyst use); USES (Uses)

(selective **labeling** and isolation of **phosphopeptides**
and applications to **proteome** anal.)
IT **51-85-4**, Cystamine **76-05-1**, Trifluoroacetic acid,
reactions **1969-54-6 7803-49-8**, Hydroxyamine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective **labeling** and isolation of **phosphopeptides**
and applications to **proteome** anal.)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr ind 1-6

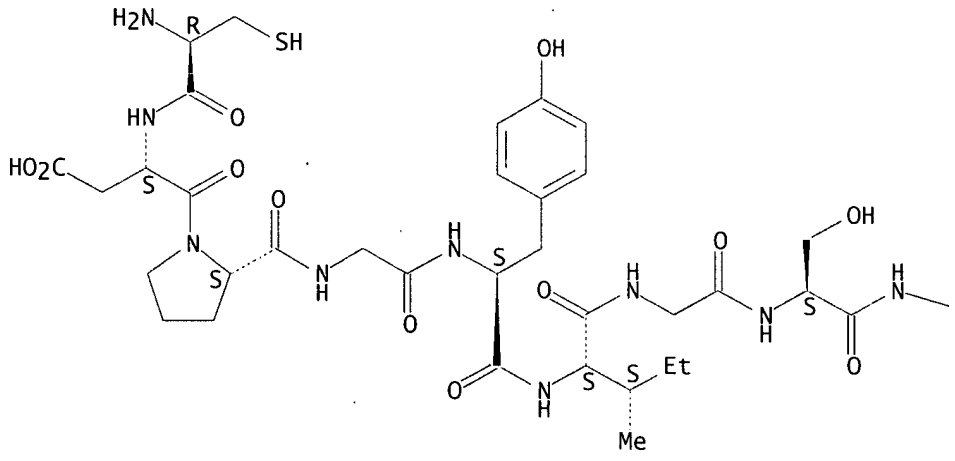
L15 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:326448 HCAPLUS
DOCUMENT NUMBER: 137:75397
TITLE: Quantitative proteome analysis by solid-phase isotope tagging and mass spectrometry
AUTHOR(S): **Zhou, H.**; Ranish, J. A.; Watts, J. D.; Aebersold, R.
CORPORATE SOURCE: Institute for Systems Biology, Seattle, WA, 98103-8904, USA
SOURCE: Nature Biotechnology (2002), 20(5), 512-515
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The adaptation of sequences of chem. reactions to a solid-phase format has been essential to the automation, reproducibility, and efficiency of a no. of biotechnol. processes including peptide and oligonucleotide synthesis and sequencing. Here we describe a method for the site-specific, stable isotopic labeling of cysteinyl peptides in complex peptide mixts. through a solid-phase capture and release process, and the concomitant isolation of the labeled peptides. The recovered peptides were analyzed by microcapillary liq. chromatog. and tandem mass spectrometry (.mu.LC-MS/MS) to det. their sequences and relative quantities. The method was used to detect galactose-induced changes in protein abundance in the yeast Saccharomyces cerevisiae. A side-by-side comparison with the isotope-coded affinity tag (ICAT) method demonstrated that the solid-phase method for stable isotope tagging of peptides is comparatively simpler, more efficient, and more sensitive.

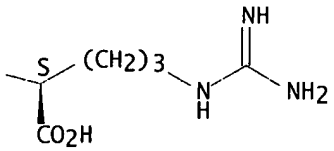
IT **110590-60-8 129785-85-9**
RL: ANT (Analyte); ANST (Analytical study)
(proteome anal. by solid-phase isotope tagging and mass spectrometry)
RN 110590-60-8 HCAPLUS
CN L-Arginine, L-cysteinyl-L-.alpha.-aspartyl-L-prolylglycyl-L-tyrosyl-L-isoleucylglycyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



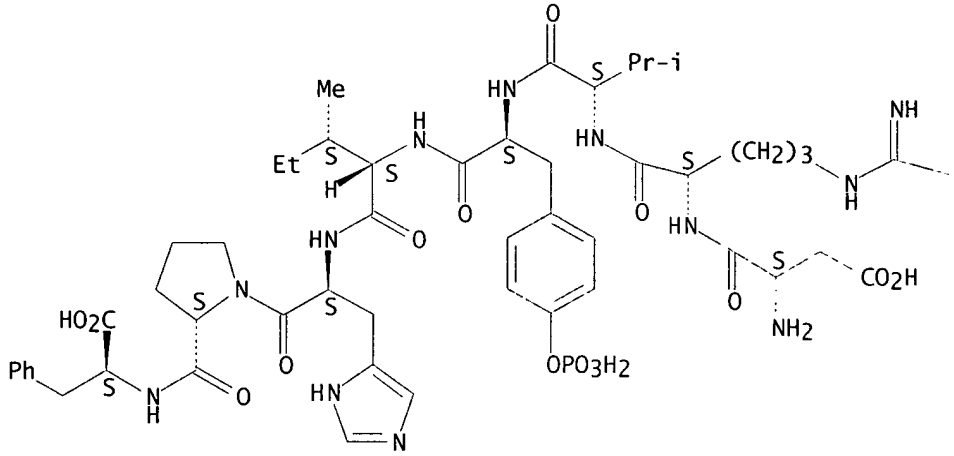
PAGE 1-B



RN 129785-85-9 HCAPLUS
CN Angiotensin II, 5-L-isoleucine-, dihydrogen phosphate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

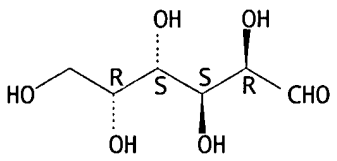


PAGE 1-B

IT **59-23-4**, D-Galactose, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(proteome anal. by solid-phase isotope tagging and mass spectrometry)
RN 59-23-4 HCAPLUS
CN D-Galactose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



CC 9-5 (Biochemical Methods)
Section cross-reference(s): 10
ST yeast proteome detn solid phase isotope tagging mass spectrometry
IT Peptides, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(cysteine-contg.; proteome anal. by solid-phase isotope tagging and mass spectrometry)
IT Peptides, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(labeled; proteome anal. by solid-phase isotope tagging and mass spectrometry)
IT Affinity
Exchange reaction
Protein sequence analysis
Saccharomyces cerevisiae
Sample preparation
Tandem mass spectrometry
(proteome anal. by solid-phase isotope tagging and mass spectrometry)
IT Proteome
RL: ANT (Analyte); ANST (Analytical study)
(proteome anal. by solid-phase isotope tagging and mass spectrometry)
IT **110590-60-8 129785-85-9**
RL: ANT (Analyte); ANST (Analytical study)
(proteome anal. by solid-phase isotope tagging and mass spectrometry)
IT **59-23-4**, D-Galactose, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(proteome anal. by solid-phase isotope tagging and mass spectrometry)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:146130 HCAPLUS
DOCUMENT NUMBER: 136:243966
TITLE: Quantitative protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry
AUTHOR(S): Smolka, Marcus; **Zhou, Huilin**; **Aebersold, Ruedi**
CORPORATE SOURCE: Departamento de Bioquimica, Instituto de Biologia, Universidade Estadual de Campinas, Sao Paulo, 13083-970, Brazil
SOURCE: Molecular and Cellular Proteomics (2002), 1(1), 19-29
CODEN: MCPOBS; ISSN: 1535-9476
PUBLISHER: American Society for Biochemistry and Molecular

Biology, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

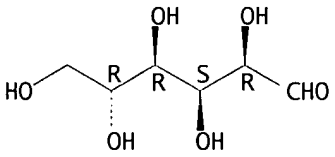
AB Quant. protein profiling is an essential part of proteomics and requires new technologies that accurately, reproducibly, and comprehensively identify and quantify the proteins contained in biol. samples. We describe a new strategy for quant. protein profiling that is based on the sepn. of proteins labeled with isotope-coded affinity tag reagents by two-dimensional gel electrophoresis and their identification and quantification by mass spectrometry. The method is based on the observation that proteins labeled with isotopically different isotope-coded affinity tag reagents precisely co-migrate during two-dimensional gel electrophoresis and that therefore two or more isotopically encoded samples can be sepd. concurrently in the same gel. By analyzing changes in the proteome of yeast (Saccharomyces cerevisiae) induced by a metabolic shift we show that this simple method accurately quantifies changes in protein abundance even in cases in which multiple proteins migrate to the same gel coordinates. The method is particularly useful for the quant. anal. and structural characterization of differentially processed or post-translationally modified forms of a protein and is therefore expected to find wide application in proteomics research.

IT **9054-89-1**, Superoxide dismutase
RL: ANT (Analyte); ANST (Analytical study)
(protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

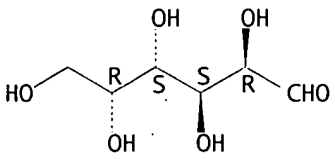
IT **50-99-7**, Glucose, analysis **59-23-4**, Galactose, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
RN 50-99-7 HCAPLUS
CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 59-23-4 HCAPLUS
CN D-Galactose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



CC 9-16 (Biochemical Methods)
ST protein profiling gel electrophoresis mass spectrometry
IT Mass spectrometry
Saccharomyces cerevisiae
Sample preparation
(protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
IT Ovalbumin
Proteome
RL: ANT (Analyte); ANST (Analytical study)
(protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
IT Albumins, analysis
RL: ANT (Analyte); ANST (Analytical study)
(serum, bovine; protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
IT Gel electrophoresis
(two-dimensional; protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
IT Lactoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(.alpha.-lactoglobulins; protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
IT Lactoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(.beta.-; protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
IT **9054-89-1**, Superoxide dismutase
RL: ANT (Analyte); ANST (Analytical study)
(protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
IT **50-99-7**, Glucose, analysis **59-23-4**, Galactose, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(protein profiling using two-dimensional gel electrophoresis, isotope-coded affinity tag labeling, and mass spectrometry)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

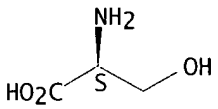
L15 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:815147 HCAPLUS
DOCUMENT NUMBER: 136:17229
TITLE: Functional interaction of calcium-/calmodulin-dependent protein kinase II and cytosolic phospholipase A2
AUTHOR(S): Muthalif, Mubarack M.; Hefner, Ying; Canaan, Stephane; Harper, Jason; **Zhou, Huilin**; Parmentier, Jean-Hugues; **Aebersold, Ruedi**; Gelb, Michael H.; Malik, Kafait U.
CORPORATE SOURCE: Department of Pharmacology, College of Medicine, The University of Tennessee, Memphis, TN, 38163, USA
SOURCE: Journal of Biological Chemistry (2001), 276(43), 39653-39660
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ca2+/calmodulin-dependent protein kinase II (CaM kinase II), a decoder of Ca2+ signals, and cytosolic phospholipase A2 (cPLA2), an enzyme involved in arachidonate release, are involved in many physiol. and pathophysiol. processes. Activation of CaM kinase II in norepinephrine-stimulated vascular smooth muscle cells leads to activation of cPLA2 and arachidonic acid release. Surface plasmon resonance, mass spectrometry, and kinetic studies showed that CaM kinase II binds to cPLA2 resulting in cPLA2 phosphorylation on Ser-515 and an increase in its enzymic activity. Phosphopeptide mapping studies with cPLA2 from norepinephrine-stimulated smooth muscle cells indicated that phosphorylation of cPLA2 on Ser-515, but not on Ser-505 or Ser-727, occurs in vivo. This novel signaling pathway for arachidonate release was shown to be cPLA2-dependent by use of a recently described and highly selective inhibitor of this enzyme.

IT **56-45-1**, L-Serine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(515; phosphorylation of phospholipase A2 on Ser-515 by calmodulin kinase II in norepinephrine-stimulated vascular smooth muscle cells leads to its activation and to arachidonate release)

RN 56-45-1 HCAPLUS
CN L-Serine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **141467-21-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(II; functional interaction of Ca2+/calmodulin-dependent protein kinase II and cytosolic phospholipase A2)

RN 141467-21-2 HCAPLUS
CN Kinase (phosphorylating), protein (calcium-calmodulin-dependent), I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9001-84-7**, Phospholipase A2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(functional interaction of Ca2+/calmodulin-dependent protein kinase II and cytosolic phospholipase A2)

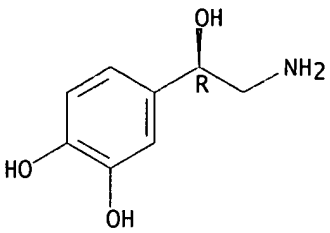
RN 9001-84-7 HCAPLUS
CN Phospholipase A2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **51-41-2**, Norepinephrine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phosphorylation of phospholipase A2 on Ser-515 by calmodulin kinase II in norepinephrine-stimulated vascular smooth muscle cells leads to its activation and to arachidonate release)

RN 51-41-2 HCAPLUS
CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 7-5 (Enzymes)
ST calmodulin kinase II interaction phospholipase A2 signal transduction
IT Molecular association
(of Ca2+/calmodulin-dependent protein kinase II and cytosolic phospholipase A2)
IT Signal transduction, biological
(phosphorylation of phospholipase A2 on Ser-515 by calmodulin kinase II in norepinephrine-stimulated vascular smooth muscle cells leads to its activation and to arachidonate release)
IT Phosphorylation, biological
(protein; of phospholipase A2 by Ca2+/calmodulin-dependent protein kinase II)
IT Blood vessel
(smooth muscle; phosphorylation of phospholipase A2 on Ser-515 by calmodulin kinase II in norepinephrine-stimulated vascular smooth muscle cells leads to its activation and to arachidonate release)
IT **56-45-1**, L-Serine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(515; phosphorylation of phospholipase A2 on Ser-515 by calmodulin kinase II in norepinephrine-stimulated vascular smooth muscle cells leads to its activation and to arachidonate release)
IT **141467-21-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(II; functional interaction of Ca2+/calmodulin-dependent protein kinase II and cytosolic phospholipase A2)
IT **9001-84-7**, Phospholipase A2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(functional interaction of Ca2+/calmodulin-dependent protein kinase II and cytosolic phospholipase A2)
IT **51-41-2**, Norepinephrine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phosphorylation of phospholipase A2 on Ser-515 by calmodulin kinase II in norepinephrine-stimulated vascular smooth muscle cells leads to its activation and to arachidonate release)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:739493 HCAPLUS
DOCUMENT NUMBER: 135:285294
TITLE: Quantitative profiling of differentiation-induced microsomal proteins using isotope-coded affinity tags and mass spectrometry
AUTHOR(S): Han, David K.; Eng, Jimmy; **Zhou, Huilin**; **Aebersold, Ruedi**
CORPORATE SOURCE: University of Connecticut Health Center, Farmington,

CT, 06030-0002, USA
SOURCE: Nature Biotechnology (2001), 19(10), 946-951
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An approach to the systematic identification and quantification of the proteins contained in the microsomal fraction of cells is described. It consists of three steps: (1) prepn. of microsomal fractions from cells or tissues representing different states; (2) covalent tagging of the proteins with isotope-coded affinity tag (ICAT) reagents followed by proteolysis of the combined labeled protein samples, and (3) isolation, identification, and quantification of the tagged peptides by multidimensional chromatog., automated tandem mass spectrometry, and computational anal. of the obtained data. The method was used to identify and det. the ratios of abundance of each of 491 proteins contained in the microsomal fractions of naive and in vitro-differentiated human myelold leukemia (HL-60) cells. The method and the new software tools to support it are well suited to the large-scale, quant. anal. of membrane proteins and other classes of proteins that have been refractory to std. proteomics technol.
CC 9-16 (Biochemical Methods)
ST microsome protein isotope affinity tag mass spectrometry
IT Proteins, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(membrane; quant. profiling of differentiation-induced microsomal proteins using isotope-coded affinity tags and mass spectrometry)
IT Computer program
Endoplasmic reticulum
Leukemia
Microsome
Protein degradation
Tandem mass spectrometry
(quant. profiling of differentiation-induced microsomal proteins using isotope-coded affinity tags and mass spectrometry)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:695694 HCAPLUS
DOCUMENT NUMBER: 135:300592
TITLE: Optimization of the isotope-coded affinity tag-labeling procedure for quantitative proteome analysis
AUTHOR(S): Smolka, Marcus B.; ~~Zhou, Huilin;~~ Purkayastha, Subhasish; ~~Aebersold, Ruedi~~
CORPORATE SOURCE: Departamento de Bioquimica, Instituto de Biologia, Universidade Estadual de Campinas, Campinas, Sao Paulo, Brazil
SOURCE: Analytical Biochemistry (2001), 297(1), 25-31
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The combination of isotope coded affinity tag (ICAT) reagents and tandem mass spectrometry constitutes a new method for quant. proteomics. It involves the site-specific, covalent labeling of proteins with isotopically normal or heavy ICAT reagents, proteolysis of the combined, labeled protein mixt., followed by the isolation and mass spectrometric

anal. of the labeled peptides. The method critically depends on labeling protocols that are specific, quant., general, robust, and reproducible. Here we describe the systematic evaluation of important parameters of the labeling protocol and describe optimized labeling conditions. The tested factors include the ICAT reagent concn., the influence of the protein, SDS, and urea concns. on the labeling reaction, and the reaction time. We demonstrate that using the optimized conditions specific and quant. labeling was achieved on std. proteins as well as in complex protein mixts. such as a yeast cell lysate. (c) 2001 Academic Press.

CC 9-5 (Biochemical Methods)

ST isotope coded affinity tag proteome analysis

IT Protein degradation
Tandem mass spectrometry
(isotope-coded affinity tag-labeling procedure for quant. proteome anal.)

IT Albumins, analysis
Ovalbumin
Proteins, general, analysis
RL: ANT (Analyte); ANST (Analytical study)
(isotope-coded affinity tag-labeling procedure for quant. proteome anal.)

IT Lactalbumins
RL: ANT (Analyte); ANST (Analytical study)
(.alpha.-; isotope-coded affinity tag-labeling procedure for quant. proteome anal.)

IT Lactoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(.beta.-; isotope-coded affinity tag-labeling procedure for quant. proteome anal.)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:260540 HCAPLUS
DOCUMENT NUMBER: 134:337879
TITLE: A systematic approach to the analysis of protein phosphorylation
AUTHOR(S): Zhou, Huilin; Watts, Julian D.; Aebersold, Ruedi
CORPORATE SOURCE: Department of Moleclular Biotechnology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Nature Biotechnology (2001), 19(4), 375-378
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

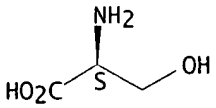
AB Time to control a wide range of biol. functions and activities1-3. Thus detn. of the site(s) of protein phosphorylation has been an essential step in the anal. of the control of many biol. systems. However, direct detn. of individual phosphorylation sites occurring on phosphoproteins in vivo has been difficult to date, typically requiring the purifn. to homogeneity of the phosphoprotein of interest before anal. Thus, there has been a substantial need for a more rapid and general method for the anal. of protein phosphorylation in complex protein mixts. Here we describe such an approach to protein phosphorylation anal. It consists of three steps: (1) selective phosphopeptide isolation from a peptide mixt. via a sequence of chem. reactions, (2) phosphopeptide anal. by automated liq. chromatog.-tandem mass spectrometry (LC-MS/MS), and (3) identification of the phosphoprotein and the phosphorylated residue(s) by correlation of tandem mass spectrometric data with sequence databases. By utilizing

various phosphoprotein stds. and a whole yeast cell lysate, we demonstrate that the method is equally applicable to serine-, threonine- and tyrosine-phosphorylated proteins, and is capable of selectively isolating and identifying phosphopeptides present in a highly complex peptide mixt.

IT **56-45-1**, L-Serine, biological studies **60-18-4**, L-Tyrosine, biological studies **72-19-5**, L-Threonine, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(phosphorylation; systematic approach to anal. of protein phosphorylation)

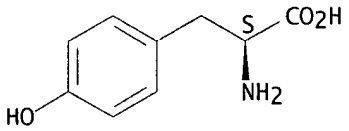
RN 56-45-1 HCAPLUS
CN L-Serine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



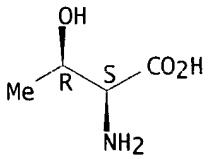
RN 60-18-4 HCAPLUS
CN L-Tyrosine (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 72-19-5 HCAPLUS
CN L-Threonine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **114051-78-4**, Protein tyrosine kinase lck
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(systematic approach to anal. of protein phosphorylation)

RN 114051-78-4 HCAPLUS
CN Kinase (phosphorylating), protein p56lck (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CC 9-16 (Biochemical Methods)
Section cross-reference(s): 6, 7, 10

ST phosphoprotein protein phosphorylation analysis liq chromatog mass

spectrometry
IT Mass spectrometry
(liq. chromatog. combined with; systematic approach to anal. of protein phosphorylation)
IT Liquid chromatography
(mass spectrometry combined with; systematic approach to anal. of protein phosphorylation)
IT Protein motifs
(phosphorylation site; systematic approach to anal. of protein phosphorylation)
IT Phosphoproteins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pp56lck; systematic approach to anal. of protein phosphorylation)
IT Phosphorylation, biological
(protein; systematic approach to anal. of protein phosphorylation)
IT Liquid chromatography
Saccharomyces cerevisiae
Tandem mass spectrometry
(systematic approach to anal. of protein phosphorylation)
IT Myelin basic protein
Phosphopeptides
Phosphoproteins
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(systematic approach to anal. of protein phosphorylation)
IT Caseins, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(.beta.-; systematic approach to anal. of protein phosphorylation)
IT **56-45-1**, L-Serine, biological studies **60-18-4**, L-Tyrosine, biological studies **72-19-5**, L-Threonine, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(phosphorylation; systematic approach to anal. of protein phosphorylation)
IT **114051-78-4**, Protein tyrosine kinase lck
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(systematic approach to anal. of protein phosphorylation)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Considered 05/01/03 MEC

=> file biosis
FILE 'BIOSIS' ENTERED AT 13:44:48 ON 02 APR 2003

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 March 2003 (20030326/ED)

=> d que l154

L124 1356 SEA FILE=BIOSIS ABB=ON PLU=ON (?PROTEIN? OR ?PEPTID? OR ANTIBOD? OR POLYPEPTID?) AND PHOSPHORAM?
L125 100 SEA FILE=BIOSIS ABB=ON PLU=ON L124 AND (PHOSPHATE OR PHOSPHORYL?)
L126 21 SEA FILE=BIOSIS ABB=ON PLU=ON L125 AND PROTECT?
L154 1 SEA FILE=BIOSIS ABB=ON PLU=ON L126 AND (PHOSPHORAMIDITE AND SOLID-PHASE)/TI 1 cite from Biosis

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 13:44:50 ON 02 APR 2003
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FILE COVERS 1907 - 2 Apr 2003 VOL 138 ISS 14
FILE LAST UPDATED: 1 Apr 2003 (20030401/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification. CT = controlled terminology

=> d que l47

L24 60578 SEA FILE=HCAPLUS ABB=ON PLU=ON CARBOXYLIC ACIDS/CT
L25 7275 SEA FILE=HCAPLUS ABB=ON PLU=ON CARBOXYL GROUP/CT
L40 455 SEA FILE=HCAPLUS ABB=ON PLU=ON (L24 OR L25)(L)PROTECT?
L47 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND ?PHOSPHORAM? 1 cite

=> d que l57

L50 125944 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPH?(5A)(PROTEIN OR ?PEPTID?)
L51 30306 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPH?(5A)(AMINO OR AMINE)

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L52        1241 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L50 OR L51) AND PHOSPHORAM?
L55        3866 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?CARBOXY?(5A)PROTECT?
L56           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L55 AND L52
L57           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L56 AND PROTECTION/TI  1 cite

=> d que l66

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L24       60578 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARBOXYLIC ACIDS/CT
L25        7275 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARBOXYL GROUP/CT
L33        1344 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHOPEPTIDES/CT
L34       65322 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLATION, BIOLOGICAL/CT

L40         455 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L24 OR L25)(L)PROTECT?
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L63          79 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L55 OR L40) AND (L50 OR L51)

L64          73 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L63 NOT PHOSPHATASE
L65           9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L22 OR (L33 OR L34)) AND L64

L66           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND (GLYCOPEPTIDE OR
                PEPTIDE SYNTHESIS)/TI     3 cites

=> d que l69

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L21      105964 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEPTIDES/CT
L22       35553 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHOPROTEINS/CT
L23      148834 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBODIES/CT
L24       60578 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARBOXYLIC ACIDS/CT
L25        7275 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARBOXYL GROUP/CT
L34       65322 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLATION, BIOLOGICAL/CT

L35       14620 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L20 OR L21) OR L23)(L)(RACT   Ract/RCT =
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L67          74 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L22 OR (L34 OR L35)) AND
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=> d que l71

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L21      105964 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEPTIDES/CT
L22       35553 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHOPROTEINS/CT
L23      148834 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBODIES/CT
L24       60578 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARBOXYLIC ACIDS/CT
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L71           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70 AND (L20 OR L21 OR L22 OR
                 L23)        2 cites

=> s l47 or l57 or l66 or l69 or l71

L155          6 L47 OR L57 OR L66 OR L69 OR L71  6 cites total from HCAPLUS

=> file scisearch

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FILE COVERS 1974 TO 28 Mar 2003 (20030328/ED)

=> d que l123

L112       1193 SEA FILE=SCISEARCH ABB=ON  PLU=ON  (?PROTEIN? OR ?PEPTID? OR
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                 RAM?
L121         36 SEA FILE=SCISEARCH ABB=ON  PLU=ON  L112 AND L120
L123          3 SEA FILE=SCISEARCH ABB=ON  PLU=ON  L121 AND (PEPTIDES OR
                 PHOSPHOPEPTIDES)/TI     3 cites from sci search

=> file wpix

FILE 'WPIX' ENTERED AT 13:44:55 ON 02 APR 2003
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FILE LAST UPDATED:          28 MAR 2003      <20030328/UP>
MOST RECENT DERWENT UPDATE:     200321        <200321/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SLART (Simultaneous Left and Right Truncation) is now
    available in the /ABEX field. An additional search field
    /BIX is also provided which comprises both /BI and /ABEX <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d que l84

L77        2958 SEA FILE=WPIX ABB=ON  PLU=ON  (?PROTEIN? OR ?PEPTID? OR
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                ANTIBOD?)(5A)PHOSPHO?
L78          213 SEA FILE=WPIX ABB=ON  PLU=ON  L77 AND PROTECT?
L79           51 SEA FILE=WPIX ABB=ON  PLU=ON  L78 AND ?CARBOXY?
L82         5452 SEA FILE=WPIX ABB=ON  PLU=ON  ?CARBOXY?(10A)(PROTECT? OR
                MASK?)
L83           15 SEA FILE=WPIX ABB=ON  PLU=ON  L79 AND L82
L84            7 SEA FILE=WPIX ABB=ON  PLU=ON  L83 AND (AEROBIC OR ALKYL-PHOSPHO
                N? OR (PHOSPHORYLATED PEPTIDES) OR ANGIOTENSIN OR ANTIBODIES
                OR CARBOXYLIC)/TI        7 cites

=> d que l89

L77         2958 SEA FILE=WPIX ABB=ON  PLU=ON  (?PROTEIN? OR ?PEPTID? OR
                ANTIBOD?)(5A)PHOSPHO?
L85           38 SEA FILE=WPIX ABB=ON  PLU=ON  L77 AND PHOSPHORAMID?
L86           17 SEA FILE=WPIX ABB=ON  PLU=ON  L85 AND ?CARBOXY?
L87            9 SEA FILE=WPIX ABB=ON  PLU=ON  L86 AND (LABEL? OR TAG OR
                TAGGING OR TAGGED)
L88          352 SEA FILE=WPIX ABB=ON  PLU=ON  PHOSPHOPROTEIN OR PHOSPHOPEPT?
                OR PHOSPHOPOLYPEPT?
L89            1 SEA FILE=WPIX ABB=ON  PLU=ON  L88 AND L87    1 cite


=> s l84 or l89

L156           7 L84 OR L89   7 cites total from WPIX(Derwent)

=> dup rem l154 l155 l123 l156   removing duplicate citations
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FILE 'WPIX' ENTERED AT 13:45:42 ON 02 APR 2003
COPYRIGHT (C) 2003 THOMSON DERWENT
PROCESSING COMPLETED FOR L154
PROCESSING COMPLETED FOR L155
PROCESSING COMPLETED FOR L123
PROCESSING COMPLETED FOR L156
L157          17 DUP REM L154 L155 L123 L156 (0 DUPLICATES REMOVED)  17 cites total
                ANSWER '1' FROM FILE BIOSIS
                ANSWERS '2-7' FROM FILE HCAPLUS
                ANSWERS '8-10' FROM FILE SCISEARCH
                ANSWERS '11-17' FROM FILE WPIX

=> d ibib abs

L157 ANSWER 1 OF 17  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:    2000:313652  BIOSIS
DOCUMENT NUMBER:     PREV200000313652
TITLE:               Preparation of an asymmetrically protected
                     phosphoramidite and its application in
                     solid-phase synthesis of
```

phosphopeptides.
AUTHOR(S): Kupihar, Zoltan; Varadi, Gyorgyi; Monostori, Eva; Toth, Gabor K. (1)
CORPORATE SOURCE: (1) Department of Medical Chemistry, University of Szeged, Dom ter 8, H-6720, Szeged Hungary
SOURCE: Tetrahedron Letters, (8 June, 2000) Vol. 41, No. 22, pp. 4457-4461. print.
ISSN: 0040-4039.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB O-tert-Butyl-O'-beta-cyanoethyl-N,N-diisopropylphosphoramidite as a new global **phosphorylation** reagent and its application for solid-phase **phosphopeptide** synthesis via monoprotected **phosphate-peptide** ester during **peptide** synthesis are described.

=> d ibib abs hitrn 2-7

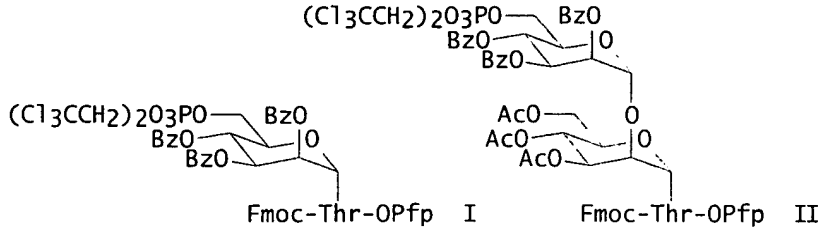
L157 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:689758 HCAPLUS
DOCUMENT NUMBER: 138:137364
TITLE: A new synthesis of **phosphoramidates**: inhibitors of the key bacterial enzyme aspartate semi-aldehyde dehydrogenase
AUTHOR(S): Adams, Luke A.; Cox, Russell J.; Gibson, Jennifer S.; Mayo-Martin, M. Belen; Walter, Magnus; Whittingham, William
CORPORATE SOURCE: School of Chemistry, University of Bristol, Bristol, BS8 1TS, UK
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2002), (18), 2004-2005
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new, mild and high yielding synthesis of **phosphoramidates** (EtO)2PONHCOR is described: potassium salts of carboxylic acids RCO2K are treated with ethylchloroformate and the resulting activated anhydride-carbonates are then treated with LiNHP(O)(OEt)2 in situ. This methodol. is esp. suited to acid sensitive systems featuring BOC, tBu or acetal protecting groups. 4-**Aspartylphosphoramide** (2S)-(HO)2PONHCOCH2CHNH2CO2H (4) was prepd. from (2S)-MeO2CH2CHN(BOC)2CO2tBu and has shown high activity in inhibition of the title enzyme (ASA-DH). Mol. modeling studies support the obsd. lack of a covalent binding of 4 to the active site of ASA-DH.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L157 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:25007 HCAPLUS
DOCUMENT NUMBER: 136:263406
TITLE: ~~**Peptide synthesis**~~
AUTHOR(S): ~~Elmore, Donald T.~~
CORPORATE SOURCE: University of Oxford, Oxford, UK
SOURCE: Amino Acids, Peptides, and Proteins (2001), 32, 107-162
CODEN: AAPPFP; ISSN: 1361-5904
PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with many refs. Several aspects of peptide synthesis are discussed: **protection** of amino groups, **protection** of **carboxy** groups, **protection** of amino acid side chains, disulfide bond formation, peptide bond formation, solid-phase peptide synthesis, enzyme-mediated peptide synthesis, and purifn. methods. This review categorizes the refs. (primarily from 1999) in terms of their contents, such as different kinds of biol. important peptides and their biol. activities.
REFERENCE COUNT: 784 THERE ARE 784 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L157 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:589767 HCAPLUS
DOCUMENT NUMBER: 129:290406
TITLE: Preparation of **phosphate**-linked nucleotide-**amino** acid and -**peptide** conjugates via the **phosphoramidite** approach with allyl/allyloxycarbonyl **protection**
AUTHOR(S): Sakakura, Akira; Hayakawa, Yoshihiro
CORPORATE SOURCE: Graduate School of Human Informatics, Nagoya University, Chikusa, Nagoya, 464-8601, Japan
SOURCE: Nucleic Acids Symposium Series (1998), 39, 25-26
CODEN: NACSD8; ISSN: 0261-3166
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new way to nucleotide-peptide hybrids in which the two components was connected by the phosphate linkage has been opened via the **phosphoramidite** method using allyl and allyloxycarbonyl groups for **protection** of the **phosphoric** or **carboxylic** acid moiety and **amino** function, resp.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L157 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:123443 HCAPLUS
DOCUMENT NUMBER: 126:238638
TITLE: Constrained **glycopeptide** ligands for MPRs. Limitations of unprotected phosphorylated building blocks
AUTHOR(S): Franzyk, Henrik; Christensen, Mette K.; Joergensen, Rikke M.; Meldal, Morten; Cordes, Henriette; Mouritsen, Soeren; Bock, Klaus
CORPORATE SOURCE: Carlsberg Laboratory, Department of Chemistry, Valby, DK-2100, Den.
SOURCE: Bioorganic & Medicinal Chemistry (1997), 5(1), 21-40
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A new methodol. for the synthesis of cyclic and **phosphorylated glycopeptide** templates was developed. First, fully protected building blocks I and II (Fmoc = 9-fluorenylmethoxycarbonyl; Pfp = C6F5) contg. mannose and mannose disaccharides with bis-trichloroethyl phosphate protective groups were synthesized. These were used in solid-phase assembly through side chain anchoring of glycosylated hexa- and octapeptides **protected** at the C-terminal **carboxylate** as the allyl ester. Selective allyl ester cleavage and head-to-tail cyclization under pseudo-diln. conditions gave a high yield of pure cyclic peptide templates. An unprotected phosphate building block was evaluated as an alternative to the problematic trichloroethyl group. It was found that one unprotected phosphate is readily incorporated, whereas the second unprotected phosphorylated building block reacts very slowly due to electrostatic repulsion in the solid-phase synthesis. For comparison with previous binding studies, modified **glycopeptide** templates contg. only **phosphorylated** mannose monosaccharides or templates modified in the peptide part were synthesized. All the structures were tested for their binding to the mannose 6-phosphate receptor, and it was found that although mannose disaccharides are required for optimal interaction, the detailed structure of the peptide template has a strong influence on binding to the receptor. The restricted conformations of the cyclic peptides decreased the binding considerably.

L157 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:776765 HCAPLUS
DOCUMENT NUMBER: 123:340935
TITLE: Preparation of O-phosphotyrosine-containing peptides by Fmoc solid-phase synthesis: evaluation of several Fmoc-Tyr(PO3R2)-OH derivatives
AUTHOR(S): Valerio, R. M.; Bray, A. M.; Maeji, N. J.; Morgan, P. O.; Perich, J. W.
CORPORATE SOURCE: Chiron Mimotopes Pty. Ltd., Clayton, 3168, Australia
SOURCE: Letters in Peptide Science (1995), 2(1), 33-40
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: ESCOM
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of two model Tyr(P)-contg. peptides using Fmoc-Tyr(PO3tBu2)-OH, Fmoc-Tyr(PO3Bzl2)-OH and Fmoc-Tyr(PO3H2)-OH established that the t-butylphosphate-protected deriv. was the preferred deriv. for use in Fmoc solid-phase peptides synthesis, since it afforded phosphopeptides in high purity and with the lowest amt. of Tyr-peptide contamination. In addn., this study confirmed that com. available Fmoc-Tyr(PO3H2)-OH is also suitable for use in Fmoc solid-phase synthesis but gives less pure phosphopeptides, along with the generation of 1-4% of the tyrosine-contg. peptide for the model sequences studied. In view of the good performance of Fmoc-Tyr(PO3tBu2)-OH, a large-scale three-step synthetic procedure was developed which involved phenacyl

protection of the **carboxyl** group, phosphite-triester phosphorylation of the tyrosyl hydroxyl using di-t-Bu N,N-**diethylphosphoramidite**, and final removal of the phenacyl group by zinc redn. in acetic acid.

L157 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:194849 HCAPLUS
DOCUMENT NUMBER: 116:194849
TITLE: Further studies on the use of 2,2,2-trichloroethyl groups for **phosphate** protection in **phosphoserine peptide synthesis**
AUTHOR(S): Paquet, Alenka
CORPORATE SOURCE: Food Res. Cent., Canada, Dep. Agric., Ottawa, ON, Can.
SOURCE: International Journal of Peptide & Protein Research (1992), 39(1), 82-6
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:194849
AB Serine derivs. R-Ser (PO3Tc2)-OH [I; R = Me3CO2C (Boc), PhCH2O2C (Z), 9-fluoronylmethoxycarbonyl (Fmoc); Tc = CH2CCl3], derivs. useful for peptide synthesis, have been obtained in high yields by acylation of I (R = H).CF3CO2H. The latter was obtained from Boc- or Z-Ser(PO3Tc2)-OCH2Ph by simultaneous removal of the amino and **carboxy** **protecting** groups by Pd-catalyzed hydrogenolysis in acetic acid-trifluoroacetic acid soln. Removal of the Tc protecting group was efficiently achieved by hydrogenolysis in aq. ethanol.

=> d ibib abs 8-17

L157 ANSWER 8 OF 17 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 90:171985 SCISEARCH
THE GENUINE ARTICLE: CV497
TITLE: N,N-DIISOPROPYL-BIS(4-CHLOROBENZYL)**PHOSPHORAMIDITE** - A VERSATILE PHOSPHITYLATING AGENT FOR THE PHOSPHORYLATION OF HYDROXY **AMINO**-ACIDS AND PREPARATION OF PROTECTED **PHOSPHOPEPTIDES**
AUTHOR: DEBONT H B A (Reprint); VANBOOM J H; LISKAMP R M J
CORPORATE SOURCE: LEIDEN STATE UNIV, GORLAEUS LABS, DEPT ORGAN CHEM, POB 9502, 2300 RA LEIDEN, NETHERLANDS (Reprint)
COUNTRY OF AUTHOR: NETHERLANDS
SOURCE: RECUEIL DES TRAVAUX CHIMIQUES DES PAYS-BAS-JOURNAL OF THE ROYAL NETHERLANDS CHEMICAL SOCIETY, (1990) Vol. 109, No. 1, pp. 27-28.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: PHYS
LANGUAGE: ENGLISH
REFERENCE COUNT: 28

L157 ANSWER 9 OF 17 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 77:83842 SCISEARCH
THE GENUINE ARTICLE: CW318
TITLE: STUDIES ON INHIBITION OF THERMOLYSIN WITH **PHOSPHORAMIDATES** OF **PEPTIDES** AND **AMINO**-ACIDS
AUTHOR: KAM C M (Reprint); POWERS J C
CORPORATE SOURCE: GEORGIA INST TECHNOL, ATLANTA, GA, 30332
COUNTRY OF AUTHOR: USA

SOURCE: FEDERATION PROCEEDINGS, (1977) Vol. 36, No. 3, pp. 766.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: ENGLISH
REFERENCE COUNT: 1

L157 ANSWER 10 OF 17 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 76:234162 SCISEARCH
THE GENUINE ARTICLE: BW219
TITLE: CYCLIC **PHOSPHORAMIDE** MUSTARD (NSC-69945) DERIVATIVES OF **AMINO**-ACIDS AND **PEPTIDES**
AUTHOR: SZEKERKE M (Reprint)
CORPORATE SOURCE: EOTVOS UNIV, INST ORG CHEM, BUDAPEST 1088, HUNGARY
COUNTRY OF AUTHOR: HUNGARY
SOURCE: CANCER TREATMENT REPORTS, (1976) Vol. 60, No. 4, pp. 347-354.
DOCUMENT TYPE: Article; Journal
LANGUAGE: ENGLISH
REFERENCE COUNT: 22

L157 ANSWER 11 OF 17 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-122223 [16] WPIX
DOC. NO. NON-CPI: N2002-091676
DOC. NO. CPI: C2002-037465
TITLE: Selective **labelling** of phosphate groups in peptides and proteins for separation, isolation and detection of **phosphoproteins** and **phosphopeptides**, comprises the presence of **carboxylic** acids.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): AEBERSOLD, R; ZHOU, H
PATENT ASSIGNEE(S): (UNIW) UNIV WASHINGTON; (AEBE-I) AEBERSOLD R; (ZHOU-I) ZHOU H
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001096869	A1	20011220	(200216)*	EN	59

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001066894 A 20011224 (200227)
US 2002049307 A1 20020425 (200233)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001096869	A1	WO 2001-US18988	20010612
AU 2001066894	A	AU 2001-66894	20010612
US 2002049307	A1 Provisional	US 2000-210972P	20000612
		US 2001-880713	20011018

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2001066894 A Based on WO 200196869

PRIORITY APPLN. INFO: US 2000-210972P 20000612; US 2001-880713 20011018
AN 2002-122223 [16] WPIX
AB WO 200196869 A UPAB: 20020308
NOVELTY - Selective **labelling** phosphate groups in peptides or proteins in the presence of **carboxylic** acid groups, is new.
DETAILED DESCRIPTION - Selective **labelling** phosphate groups in peptides or proteins in the presence of **carboxylic** acid groups comprises:
(1) reacting the substrate to **protect** the phosphates as **phosphoramides** and the **carboxylates** as amides;
(2) selectively cleaving the **phosphoramide** bonds; and
(3) reacting the free phosphates with a **label** or **tag**.
INDEPENDENT CLAIMS are included for the following:
(1) detecting **phosphopeptides** in samples containing a mixture of peptides comprising:
(a) selective **protection** of **carboxyl** groups;
(b) selective **labelling** of phosphate groups; and
(c) detection of the **labelled** peptides;
(2) a kit for selectively **labelling phosphopeptides** in a mixture of **peptides** comprising:
(a) a **protective** group which reacts with a **carboxylic** acid or ester and a phosphate group; and
(b) a mild reagent for selectively regenerating any free phosphate groups in the peptide by reacting the **protected** peptides under mild acid conditions so that the **phosphoramide** bond is cleaved and the amide bonds is not cleaved.
USE - The new method is used for selectively **labelling** phosphate groups in peptides or proteins in the presence of **carboxylic** acid groups (claimed). It is useful in separation, isolation and detection of **phosphoproteins** and **phosphopeptides**.
Dwg.0/6

L157 ANSWER 12 OF 17 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1997-100960 [10] WPIX
DOC. NO. CPI: C1997-032377
TITLE: Prepn. of alpha-N,N-di alkyl-amino-**carboxylic** acid amide derivs. - from amino acid and amine with **alkyl-phosphonic** acid anhydride, useful as intermediates in peptide synthesis of enkephalin and dolastatin cpds..
DERWENT CLASS: B02 B05
INVENTOR(S): BUSCHMANN, E; ZIERKE, T
PATENT ASSIGNEE(S): (BADI) BASF AG
COUNTRY COUNT: 40
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19527574	A1	19970130	(199710)*		6
WO 9705096	A1	19970213	(199713)	GE	16
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU BG BR CA CN CZ HU IL JP KR MX NO NZ PL SG SK TR UA US					
AU 9666155	A	19970226	(199725)		
ZA 9606372	A	19980325	(199819)		12
EP 842142	A1	19980520	(199824)	GE	

R: AT BE CH DE ES FI FR GB IT LI NL SE
CZ 9800089 A3 19980617 (199830)
HU 9802403 A2 19990301 (199916)
AU 704270 B 19990415 (199926)
US 5945543 A 19990831 (199942)
JP 11509851 W 19990831 (199946) 15
KR 99035976 A 19990525 (200032)
IL 122397 A 20000928 (200063)
TW 403733 A 20000901 (200112)
EP 842142 B1 20010926 (200157) GE
R: AT BE CH DE ES FI FR GB IT LI NL SE
DE 59607794 G 20011031 (200173)
ES 2164259 T3 20020216 (200222)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 19527574	A1	DE 1995-19527574	19950728
WO 9705096	A1	WO 1996-EP3075	19960712
AU 9666155	A	AU 1996-66155	19960712
ZA 9606372	A	ZA 1996-6372	19960726
EP 842142	A1	EP 1996-925746	19960712
		WO 1996-EP3075	19960712
CZ 9800089	A3	WO 1996-EP3075	19960712
		CZ 1998-89	19960712
HU 9802403	A2	WO 1996-EP3075	19960712
		HU 1998-2403	19960712
AU 704270	B	AU 1996-66155	19960712
US 5945543	A	WO 1996-EP3075	19960712
		US 1998-983287	19980120
JP 11509851	W	WO 1996-EP3075	19960712
		JP 1997-507162	19960712
KR 99035976	A	WO 1996-EP3075	19960712
		KR 1998-700637	19980126
IL 122397	A	IL 1996-122397	19960712
TW 403733	A	TW 1996-108766	19960719
EP 842142	B1	EP 1996-925746	19960712
		WO 1996-EP3075	19960712
DE 59607794	G	DE 1996-507794	19960712
		EP 1996-925746	19960712
		WO 1996-EP3075	19960712
ES 2164259	T3	EP 1996-925746	19960712

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9666155	A	Based on	WO 9705096
EP 842142	A1	Based on	WO 9705096
CZ 9800089	A3	Based on	WO 9705096
HU 9802403	A2	Based on	WO 9705096
AU 704270	B	Previous Publ.	AU 9666155
		Based on	WO 9705096
US 5945543	A	Based on	WO 9705096
JP 11509851	W	Based on	WO 9705096
KR 99035976	A	Based on	WO 9705096
EP 842142	B1	Based on	WO 9705096
DE 59607794	G	Based on	EP 842142
		Based on	WO 9705096

ES 2164259 T3 Based on EP 842142

PRIORITY APPLN. INFO: DE 1995-19527574 19950728
AN 1997-100960 [10] WPIX
AB DE 19527574 A UPAB: 19970307
Prepn. of alpha -(N,N-dialkylamino)**carboxylic** acid amides of formula (R2)(R3)NCH(R1)CONR4R5 (I) comprises reaction of free acids of formula (R2R3N)CH(R1)(COOH) (II) with primary or secondary amines of formula NHR4R5 (III) in the presence of an alkylphosphonic acid anhydride. R1 = 1-6C alkyl, 3-7C cycloalkyl, Ph, CH2Ph, (CH2)3NH(C=NH)NH2, CH2CONH2, CH2COOH, CH2SH, (CH2)2CONH2, (CH2)2COOH, imidazolyl-5-methylene, (CH2)4NH2, (CH2)2SMe, CH2OH, CH(OH)Me or indolyl- beta -methylene, where reactive groups may, if necessary, be **protected**; R2 = 1-6C alkyl or opt. substd. benzyl; R3 = 1-6C alkyl, opt. substd. benzyl, or R1 and R3 may be bonded to each other; R4, R5 = 1-6C alkyl or 3-7C cycloalkyl or Ph, aromatic heterocycle or benzyl (each opt. substd. by 1-3 F, Cl, Br, 1-5C alkyl, 1-5C alkoxy or CF3); or NR4R5 = amino acid or peptide residue. The **carboxyl** group and other functional groups may be **protected**.

USE - (I) are useful as intermediates in the synthesis of peptides with interesting pharmacological properties e.g. enkephalins and dolastatins. Dolastatin 10 shows antineoplastic activity.

ADVANTAGE - The process gives better yields than previous methods.

Dwg.0/0

L157 ANSWER 13 OF 17 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1994-313704 [39] WPIX
DOC. NO. CPI: C1994-142851
TITLE: New phosphorylated amino acid derivs - are useful for prepn. of **antibodies** for diagnosis of various diseases.
DERWENT CLASS: B04 B05
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 06239884	A	19940830	(199439)*		13

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 06239884	A	JP 1993-262487	19931020

PRIORITY APPLN. INFO: JP 1992-282050 19921020; JP 1992-342118 19921222; JP 1992-342871 19921222
AN 1994-313704 [39] WPIX
AB JP 06239884 A UPAB: 19941122
Phosphorylated amino acid derivs. of formula R1-NHCH(COR2)-X-OP(O)(OCH2CH=CH2)2 (I) are new. In (I), R1 = amino **protecting** gp., opt. **protected** aminoacid residue or peptide residue; R1 = OR3 or R4; R3 = H or **carboxy protecting** gp.; R4 = opt. **protected** aminoacid residue or peptide residue; X = divalent hydrocarbyl.

Also new are N(alpha)-t-butoxycarbonyl- O-diallylphosphonyl-serine ditolyl methyl ester; and N(alpha)-t-butoxycarbonyl- O-diallylphosphoryl-serine.

USE/ADVANTAGE - (I) are useful for the prepn. of antibodies which are used in the diagnosis of various diseases in the early stage. The antibodies are prepd. efficiently from (I).
Dwg.0/0

L157 ANSWER 14 OF 17 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1986-091233 [14] WPIX
DOC. NO. CPI: C1986-038952
TITLE: **Phosphorous**-containing **peptide** derivatives - useful as inhibitors of **angiotensin** converting enzyme.
DERWENT CLASS: B05
PATENT ASSIGNEE(S): (KYOW) KYOWA HAKKO KOGYO KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 61037790	A	19860222	(198614)*		4

PRIORITY APPLN. INFO: JP 1984-162379 19840731
AN 1986-091233 [14] WPIX
AB JP 61037790 A UPAB: 19930922
Phosphorus-contg. **peptide** derivs. of formula (I) and their salts are new (R1 is lower alkyl; X is **carboxyl**, hydroxymethyl, -COOR2 (R2 is lower alkyl, (un)substd. aryl or aralkyl), -CH2OR2 or -CH2OCOR3 (R3 is H, lower alkyl, (un)substd. aryl or aralkyl).
(I) can be prepd. by reacting cpds. (II) and (III) forming cpd. (IV) and then treating (IV) to obtain (I) (Y is a **protecting** gp. for the phenolic hydroxy; Z is lower alkyl; X' is X, provided that when X contains amino or carboxy, such group is protected).
The reaction of (II) with (III) is effected in a solvent at 0 deg.C to room temp. for 1-15 hrs. Examples of solvents are ethyl acetate. THF, dioxan, chloroform, dichloromethane, acetone, N,N-dimethylformamide and pyridine. When (II) contains **protected** amino or **protected carboxy**, the condensed prod. is deprotected with an alkali or an acid to give (IV). Treatment of (IV) with HBr/acetic acid or trifluoroacetic acid at room temp. for 3-15 hrs. gives (I).
USE - (I) show excellent inhibitory action against angiotensin converting enzyme and can be used as hypotensive agents.
0/0

L157 ANSWER 15 OF 17 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1981-91195D [50] WPIX
TITLE: Optically active **carboxylic** acid e.g. peptide amide prodn. - by reaction with di amido-phosphoric acid aryl ester in aprotic solvent in the presence of tert. amine.
DERWENT CLASS: B05
INVENTOR(S): FISCHER, G
PATENT ASSIGNEE(S): (NEUB-I) NEUBERT K
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DD 150742	A	19810916	(198150)*		11

PRIORITY APPLN. INFO: DD 1980-220578 19800421
AN 1981-91195D [50] WPIX
AB DD 150742 A UPAB: 19930915
In a new process for the amidation of optically active **carboxylic** acids (esp. amino acids and peptides) which additional functional qroups are selectively **protected**, the **carboxylic** acid is agitated in the presence of at least one equivalent of a diamidophosphoric acid aryl ester (pref. diamidophosphoric acid phenyl ester) and one equivalent of a tertiary base (esp. imidazole) in an aprotic organic solvent at room or elevated temp. (pref.at 40 deq.C), and after completion of the amidation the **protecting** groups are opt. partially or completely removed by conventional methods.

The products are useful as pharmaceuticals or intermediates for therapeutically useful substances. Simple, single step reaction which proceeds with retention of configuration.

L157 ANSWER 16 OF 17 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1980-42114C [24] WPIX
TITLE: **Phosphorus**-contg. di **peptide** with herbicidal and fungicidal activity - can be prepd. by **aerobic** cultivation of Strepiumyces microorganism.
DERWENT CLASS: C01
PATENT ASSIGNEE(S): (MEIJ) MEIJI SEIKA KAISHA
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 55007237	A	19800119	(198024)*		
JP 61045638	B	19861008	(198644)		

PRIORITY APPLN. INFO: JP 1978-79750 19780703
AN 1980-42114C [24] WPIX
AB JP 55007237 A UPAB: 19930902
Phosphorus-contg. cpd. of formula: HO-P(=O)(Me)-CH2-CH2-CH(NH2)CONH-CHR-CO2H (I). (where R is H or Me) and its salt are novel. Prepn. of (I) comprises reacting a cpd. of formula: R2O-P(=O)(Me)-CH2CH2-CH(NHR1)-CO2H (II) (where R1 is amino-**protecting** gp; R2 is phosphoric acid-**protecting** gp.) or its reactive **carboxylic** acid deriv. with a cpd. of formula H2N-CHR-CO2R3 (III) (where R is H or Me; R3 is H or **carboxylic** acid-**protecting** gp.) to produce a cpd. of formula R2/-P-(=C)(Me)CH2CH2-CH(NHR1)-CONH-CHR-CO2R3 (IV), and then eliminating from this cpd. the amino-**protecting** gp., **carboxylic** acid-**protecting** gp. and phosphoric acid-**protecting** gp. to produce (I). Prepn. alternatively of (I) (where R is Me) comprises culturing microorganism belonging to the genus of Streptomyces under aerobic conditions, and recovering (I) from the culture liq.

(I) is effective against annual weeds, perennial weeds, and shrubs. It shows contact effect and translocating effect. It can also be applied to aquatic plant. it can be smoothly inactivated in soil and does not adversely effect crops. Further, it effectively controls blast and sheath blight of rice.

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ACCESSION NUMBER: 1971-72282S [45] WPIX
TITLE: **Phosphorylated peptides** prodn.
DERWENT CLASS: B04
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 46038485	B		(197145)*		

PRIORITY APPLN. INFO: JP 1967-64889 19671009
AN 1971-72282S [45] WPIX
AB JP 71038485 B UPAB: 19930831
Process for preparing polypeptides comprises reacting a hydroxyl-amino acid or its peptide where the hydrogen atom of the hydroxyl gp. is substd. by a gp. of formula: (where X and Y are OH or an OH gp. substd. by a phenyl, benzyl or cyanomethyl gp.) with an amino acid or a peptide not having the gp. (I), where the amino gp. of one of the starting materials is free, and the carboxyl gp. is opt. **protected**, and the **carboxyl** gp. of the other starting material is activated and the amino gp. is **protected**. Examples of the hydroxy-amino acid are serine, tyrosine, oxyproline, homoserine, alpha-methylserine and delta-oxylysine.

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